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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/589,851 | 06/04/2007 | John Trowsdale | CEJ-001US | 3667 |

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| EXAMINER | |
|---|---|
| SZPERKA, MICHAEL EDWARD | |
| ART UNIT | PAPER NUMBER |
| 1644 | |
| MAIL DATE | DELIVERY MODE |
| 07/15/2010 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/589,851 | TROWSDALE ET AL. | |
| | Examiner | Art Unit | |
| | MICHAEL SZPERKA | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *26 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-43 and 45* is/are pending in the application.

4a) Of the above claim(s) *1-15,18,19,24-43 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,17 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/17/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *sequence alignments*.

## DETAILED ACTION

1. Applicant's response and election received April 26, 2010 is acknowledged.

Claims 44, 46, and 47 have been canceled.
Claims 1-43 and 45 are pending in the instant application.
Claims 1-15, 24-43, and 45 stand withdrawn from consideration as being drawn to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03, for reasons of record set forth in the restriction requirement mailed October 7, 2009.

Applicant's election without traverse of the species of bowel cancer in the reply filed on April 26, 2010 is acknowledged.

Claims 18 and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 26, 2010

Claims 16, 17, and 20-23 are under examination in the instant office action as they read on detecting the disease condition bowel cancer by detecting RAET1G polypeptides in a patient sample.

### *Information Disclosure Statement*

2. The IDS form received 8/17/06 is acknowledged and has been considered.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically claim 21 recites that the detected molecule is SEQ ID NO:1, and this claim depends from claim 20, which recites that the detected molecule must be soluble. SEQ ID NO:1 is 333 amino acids in length, and page 7 of the specification indicates that the transmembrane domain is located at residues 227-242 and that the cytoplasmic domain is residues 243-297. As such, the polypeptide of SEQ ID NO:1 comprises transmembrane and cytoplasmic domains and thus it does not appear possible that SEQ ID NO:1 can be a soluble molecule. Note that the claim recites that "the polypeptide consists of the amino acid sequence set forth in SEQ ID NO:1" and thus it does not appear that the claim encompasses truncations of SEQ ID NO:1, such as just the extracellular domain. Since the limitations recited in the claim appear to contradict the teachings of the specification, an artisan cannot reasonably know the metes and bounds of what applicant is trying to claim.

### *Claim Rejections - 35 USC § 102*

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 16, 17, and 20-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Cosman et al. (US 6,653,447) as evidenced by Benjamin et al. (US 2005/0118586) and as evidenced by Ohashi et al.

Cosman et al. disclose methods of diagnosing cancer by detecting the presence of ULBP2 polypeptides in patient samples using antibodies (see entire document, particularly the abstract and columns 38 and 39). They disclose that ULBP2 is GPI anchored, and that it exists in both membrane-anchored and soluble forms (see particularly columns 16-21 and claim 11 of Cosman et al. and paragraphs [0554-0577], most particularly [0557] of Benjamin et al.). Notably, the antibody-based detection

methods of Cosman are disclosed as detecting soluble forms in blood and other bodily fluids (see particularly lines 44-67 of column 39).

It is noted that the molecules detected by the methods of Cosman et al. are identified as ULBP2 and not as RAET1G. However, the instant specifications indicate that RAET1G polypeptides are at least 87% similar to SEQ ID NOs:1 or 2 (see particularly page 3 of the specification), and the ULBP2 polypeptide of Cosman et al. meets this threshold and is thus a "RAET1G polypeptide" (see enclosed sequence alignment as well as figure 7 of the instant invention). Further, due to the very high level of sequence identity, antibody crossreactivity is expected between ULBP2 and RAET1G because the same epitopes are present in both molecules. Indeed, Ohashi et al. have confirmed that antibodies to ULBP2 also bind RAET1G "because their extracellular domains are almost identical to each other" (see particularly Figure 1 and the left column of page 16410 of Ohashi et al.). Thus, practicing the methods of Cosman et al. will inherently also detect the presence of RAET1G in patient samples. Note that antibodies are specific for epitopes, not whole polypeptides. Thus, antibodies which bind ULBP2 will also bind a polypeptide consisting of SEQ ID NO:1 and a polypeptide consisting of SEQ ID NO:2 since all of these peptides share epitopes as evidenced by Ohashi et al.

Therefore, the prior art anticipates the claimed invention.

7. Claims 16, 17, and 20-23 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 03/054152 as evidenced by Ohashi et al.

The '152 document discloses the identification of a polypeptide which is 96% identical to SEQ ID NO:2 of the instant invention (see entire document and the enclosed sequence alignment). This polypeptide is disclosed as being detected in patient samples for the diagnosis of various cancers, including colon cancer and colorectal cancer (see particularly pages 4, 7, 61-63, and 100-102). Antibodies are disclosed as preferred embodiments for how detection in patient samples is to occur (see particularly pages 84-97 and page 101). Specifically disclosed patient samples include sputum, blood, serum, plasma, and urine. Note that serum, plasma, and urine are acellular, and

thus the detected polypeptide must be a soluble molecule. Further, the polypeptide of the '152 document is disclosed as lacking a transmembrane domain (see page 1130 and note the lack of an entry for polypeptide # 1184). Polypeptide #1184 is further disclosed as comprising MHC class I domains (see pages 456 and 479) and that its sequence is very highly homologous to ULBP2 (see pages 156 and 252).

It is noted that the polypeptide detected by the methods of the '152 document is not identified as RAET1G. However, the instant specifications indicate that RAET1G polypeptides are at least 87% similar to SEQ ID NOs:1 or 2 (see particularly page 3 of the specification), and polypeptide #1184 is well above this threshold and thus is a "RAET1G polypeptide". Further, due to the very high level of sequence identity, antibody crossreactivity is expected between polypeptide #1184 and SEQ ID NOs:1 and 2 of the instant application because the same epitopes are present in both molecules (note that SEQ ID NO:2 is a shorter splice variant of SEQ ID NO:1 and that the amino acids of the extracellular domains are essentially identical as can be seen by inspection of Figure 7 of the instant application). Indeed, Ohashi et al. have confirmed that antibodies to ULBP2, a polypeptide which comprises less sequence identity to SEQ ID NO:2 than polypeptide #1184, also bind RAET1G "because their extracellular domains are almost identical to each other" (see particularly Figure 1 and the left column of page 16410 of Ohashi et al.). Thus, practicing the methods of the '152 application will inherently also detect the presence of SEQ ID NOs:1 and 2 in patient samples. Note that antibodies are specific for epitopes, not whole polypeptides. Thus, antibodies which bind polypeptide #1184 will also bind a polypeptide consisting of SEQ ID NO:1 and a polypeptide consisting of SEQ ID NO:2 since all of these peptides share epitopes.

Therefore, the prior art anticipates the claimed invention.

8. No claims are allowable.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL SZPERKA whose telephone number is (571)272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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